REMARKS

The title has been amended to be consistent with the title set forth in the application and in the Declaration and Power of Attorney. In addition, the Abstract has been amended to comply with M.P.E.P. §608.01(b). Finally, claims 1, 3, 5, 6, and 7 have been amended for clarity. No amendments were made in view of the cited prior art.

Applicants' invention, as set forth in claim 1, relates to a coating dispersion soluble in the lower digestive tract comprising a hydroxypropyl methylcellulose acetate succinate soluble at around pH 7, an acid, a plasticizer and an anion surfactant, wherein the hydroxypropyl methylcellulose acetate succinate has an average particle size of 10 μm or less which is dispersed at a concentration of from 2 to 20 % by weight in water, and the acid is present in an amount of from 1 to 10 parts by weight per 100 parts by weight of the hydroxypropyl methylcellulose acetate succinate.

The present invention also provides, as set forth in claim 7, a coated granule for delivery to the large intestine, which comprises a medicament-containing granular core that is coated with the coating dispersion soluble in the lower digestive tract.

The present invention thus provides a coated preparation for oral administration which can release medicament even in the lower digestive tract, i.e., in the large intestine when administered orally, and to provide a coating dispersion soluble in the lower digestive tract suitable for achieving such a purpose, the coating base material used therein being not immediately dissolved during passing the ileum where the pH value raises to about 7. It also provides a large intestine delivery coated granule preparation which can sufficiently release medicament in the large intestine and even after it has reached there.

In the Office Action, the Examiner rejected claims 1-8 under 35 U.S.C. §103(a) for being obvious over Maruyama et al. (EP 0 648487) in view of Eichel et al. (EP 0 391518).

Maruyama et al. discloses a dispersion of an enteric coating agent containing hydroxypropylmethyl cellulose acetate succinate (HPMCAS), a plasticizer and an anionic surfactant. However, as recognized by the Examiner, Maruyama et al. does not teach or even suggest the incorporation of an acid into the coating dispersion nor the effect thereof.

Eichel et al. discloses that an acid containing coating layer may optionally be applied onto or an acid may be included in an inner enteric coating layer of a sustained-release pharmaceutical preparation.

The Examiner therefore believes it would have been obvious to one of ordinary skill in the art to employ the acids of Eichel et al. in the coating dispersion of Maruyama et al.

In Eichel et al., it is essential to form a multi-walled coated drug, comprising an inner wall microencapsular enteric coating and an outer wall microencapsulated control coating, and it is the inner wall coating that contains the acid either layered onto it or included in it. In contrast, in applicants' invention, the acid is incorporated into the dispersion which forms the coating for the medicament. This then enables the coated preparation to deliver the medicament to the lower digestive tract, i.e., the large intestine and then release it in that region. There is no teaching in Eichel et al. that the acid on or in an inner layer would have this effect if included in the dispersion of Maruyama, because in Eichel et al. it is the outer wall microencapsular control coating

that does not readily dissolve or disperse in either the stomach or the intestines and the acid is not in this layer.

Moreover, in the present invention it is essential that the acid be present in the coating dispersion in an amount of from 1 to 10 parts by weight per 100 parts by weight of the HPMCAS. As discussed at page 7, lines 5 to 13, when the acid is used in an amount less than 1 part by weight, the coating layer of the preparation will dissolve before reaching the lower digestive tract when administered, which results in insufficient release of the active ingredient in the large intestine. On the other hand, when the amount of the acid is too much and above the upper limit, the coating base material easily aggregates, which undesirably causes an unstable coating film.

No specific range of acid is mentioned in Eichel et al, but at least as far as the Examples are concerned, the amount is beyond the range claimed; i.e., too much.

As required by M.P.E.P. §2143, one of the requirements for establishing a prima facie case of obviousness is that the cited combination of references must teach or suggest all of the claimed limitations. Neither Maruyama et al. nor Eichel et al. teach that the acid be present "in an amount of from 1 to 10 parts by weight per 100 parts by weight of the hydroxypropyl methylcellulose acetate succinate" as set forth in claim 1.

Accordingly, it is submitted that neither claim 1 nor claims 2-8 dependent therefrom can be considered obvious over the cited combination of references. Its withdrawal as a ground of rejection of the claims and their allowance is therefore requested.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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By: _____
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Attachments: **Replacement Abstract**

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